

# Complementary and Alternative Therapies for HD

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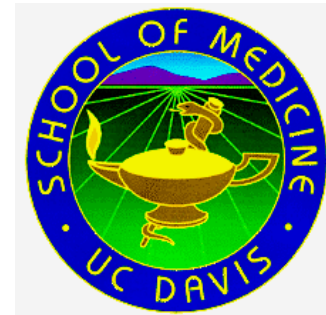
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Many of the slides presented in this  
talk were prepared  
by

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**HDSA Center of Excellence**  
**at UC Davis**



# Outline

- Definitions - CAM
- HD treatment, an integrative approach
  - Spirituality
  - Exercise
  - Diet and Supplements
  - Cautionary tales

# Complementary and Alternative Medicine (CAM):

## Definition:

“CAM is a broad domain of healing resources that encompasses all health systems, modalities, and practices and their accompanying theories and beliefs, other than those intrinsic to the dominant health system of a particular society or culture in a given historical period.”

*Source: The NIH Office of Alternative Medicine, 1994.*

# What is the “politically dominant health care system”?

Reflects broad acceptance as evidenced by “medical practice laws, legally recognized accreditation...., third party payment, privileged access to research moneys and to prestigious publication venues, high status, and so forth.”

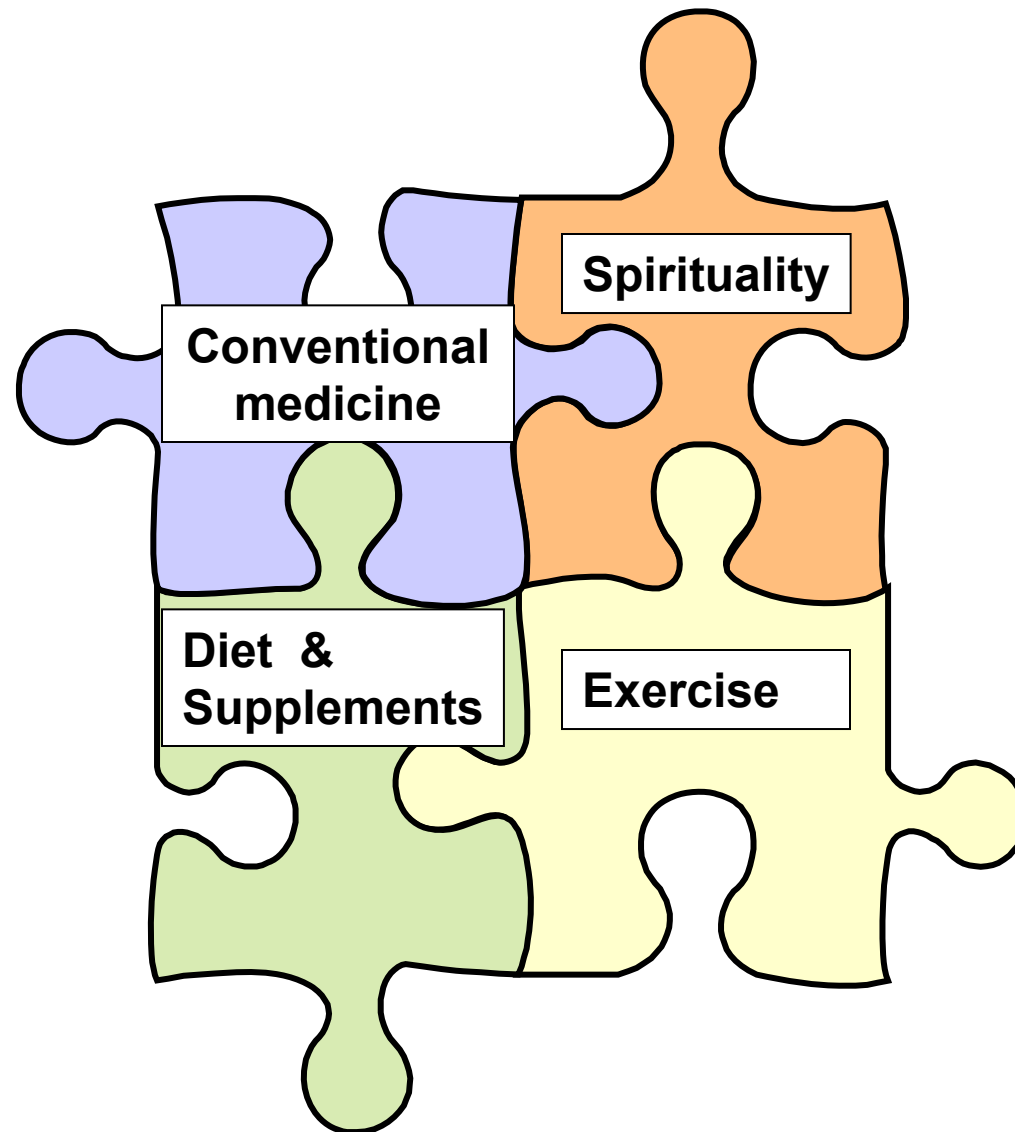
*Source: Panel on definition and description, CAM research methodology conference, Alternative Therapy 1997;3:49-57.*

# Why consider CAM for HD?

- Despite the discovery of the gene responsible for HD in 1993, we don't yet have a cure.
- Trying to stay as healthy as possible in preparation for a cure?
- Influence of predictive testing: What can a person who tests positive do while they're still healthy?

# Integrative Medicine

***Combining*** conventional and complementary treatment





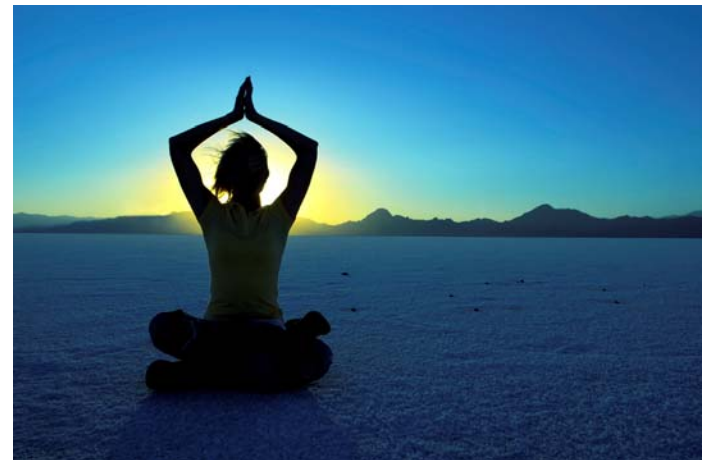
# Spirituality



Multiple paths.....

Organized religion, relaxation,  
yoga, prayer, meditation.....

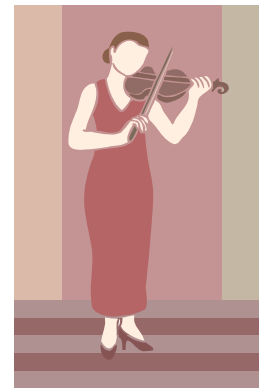
No research has been published in  
HD this area, but PHAROS and  
PREDICT studies are collecting  
data regarding practices using  
questionnaires from participants.





# “Mind-body connection techniques”

- Meditation
- Prayer
- Yoga/Tai Chi
- Biofeedback
- Hypnosis
- Relaxation therapies
  - Poetry
  - Music
  - Dance
  - Painting
  - Hobbies



# Exercise and environmental enrichment

- HD transgenic mice had delayed onset of HD symptoms when placed in a stimulating environment.
- One study of 6 individuals with HD showed behavioral improvement with re-motivation therapy



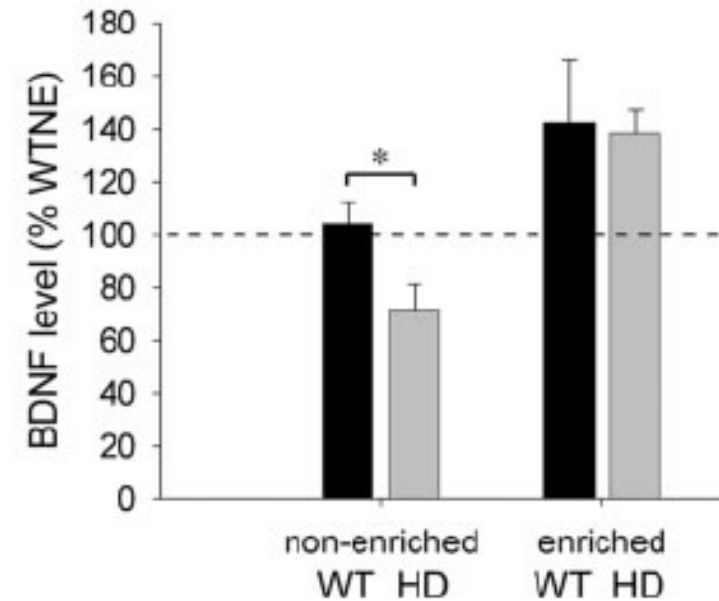
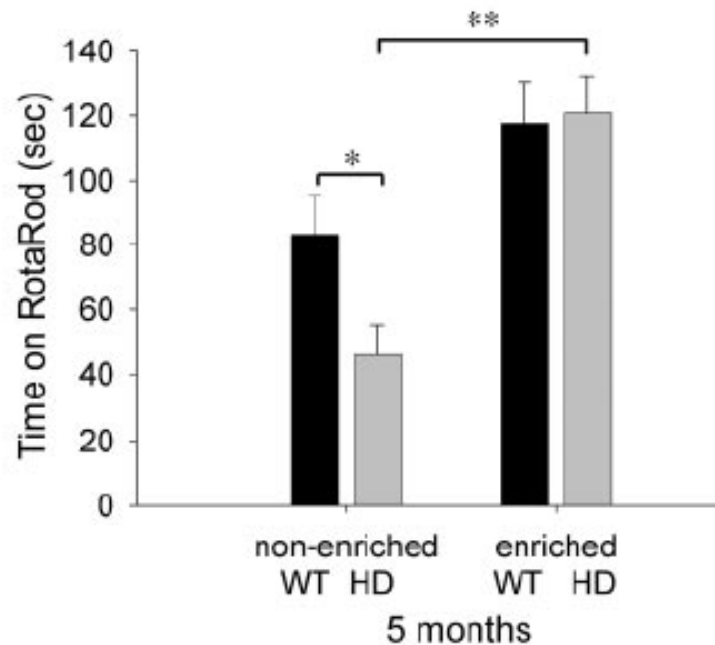
*Van Dellen et al, Nature 2000;404:721-2*  
*Sullivan et al. J Neurosci Nursing*  
*2001;33:136-142*

# Exercise

- Mechanism: explored by Spiers et al in UK:  
(J Neuroscience 2004;24:2270-6)
- Using R6/1 mouse model, mice were randomized to be placed in regular vs. enriched environments. Control mice with HD gene also used.
- Results: those in enriched environments had improved coordination and had higher levels of brain growth factors.

# Effects of enriched environment

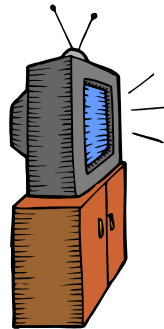
2272 • J. Neurosci., March 3, 2004 • 24(9):2270–2276



Striatal BDNF levels,  
 $p < 0.05$

**Figure 1.** Environmental enrichment enhances rotarod performance in HD and wild-type mice. At 5 months, environmental enrichment rescues an HD-induced deficit in performance on the accelerating rotarod. Bars represent *post hoc* *t* tests: \* $p < 0.05$ ; \*\* $p \leq 0.001$ .

# Effects of exercise (running)



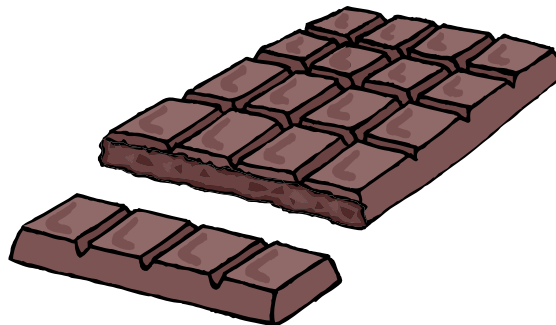
- Compared HD-model mice and wild-type mice in standard cages vs. large cages with running wheels.
- Results: Running behavior increased levels of BDNF in brains of HD mice.

# Exercise....does it help in HD?

- Possibly neuroprotective.
- Helps symptoms of pain, decreased balance, walking difficulties.
- Recommendation: exercise can be helpful but needs to be appropriate for age and fitness level.



# Diet and supplements in HD.



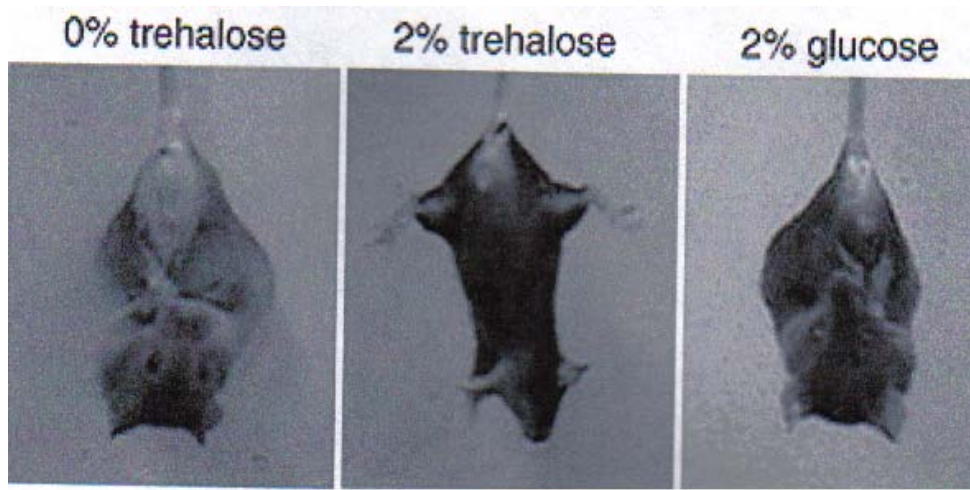
# The HD CAG expansion causes a number of metabolic changes.

- People with HD have decreased body mass index and over 3 years gain less weight than average Americans.
- Increased 24 hr energy expenditure by 11%.
- Mitochondrial energy deficit found in muscle biopsy samples from pre-symptomatic and symptomatic people with HD gene expansion.
- Cholesterol metabolism is abnormal in HD brain cells.
- Altered glucose tolerance in people with HD, diabetes in HD mice.

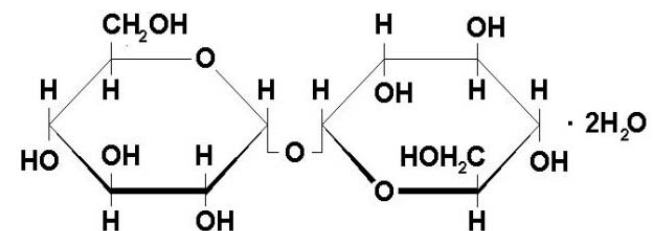


# Diet supplements in HD

- Trehalose, a naturally-occurring sugar molecule found in shellfish, honey, and mushrooms helped HD mice.



Trehalose Structure



$\alpha, \alpha$  - Trehalose

trehalose

*Tanaka et al, Nat Med 2004;10:148-54*

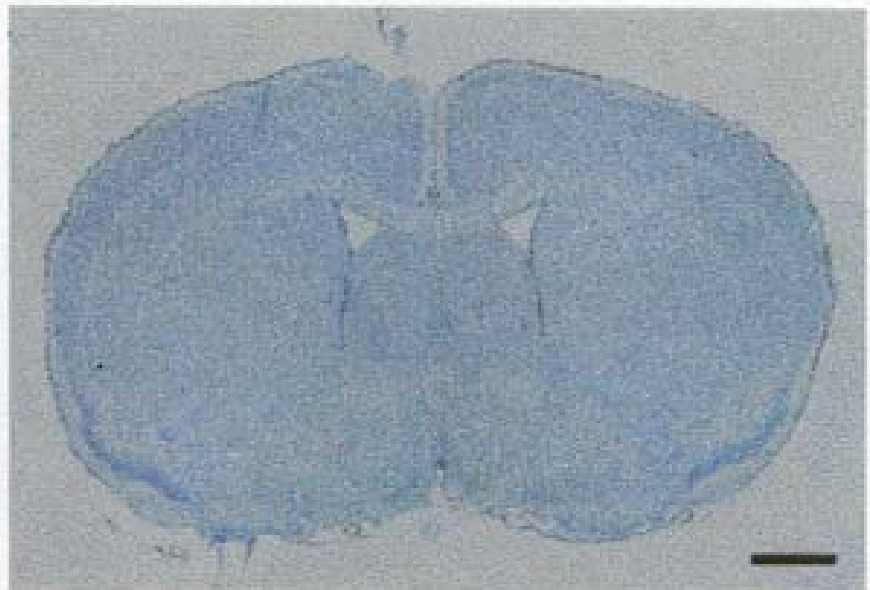
# Tanaka et al., Nature Medicine February 2004

**0% trehalose**



**Caudate loss in HD Mouse**

**2% trehalose**



**Caudate preservation in HD Mouse**

# Diet supplements



Curcumin (spice  
turmeric) reduced  
protein clumping in  
HD cells in culture



1. *Dikshit et al, BBRC 2006.*
2. *Kumar et al, Methods & Findings in Exp&Clin.Pharm. 2007*



## More diet clues



- Fruits rich in polyphenols (blueberries, cranberries, strawberries, concord grape juice) can reduce oxidative stress and brain inflammation and can improve memory and motor behavior in aged animals.
- Another polyphenol, green tea, may also help cells degrade abnormal protein

*Joseph et al, Ann NY Acad Sci 2007;1100:470-485*

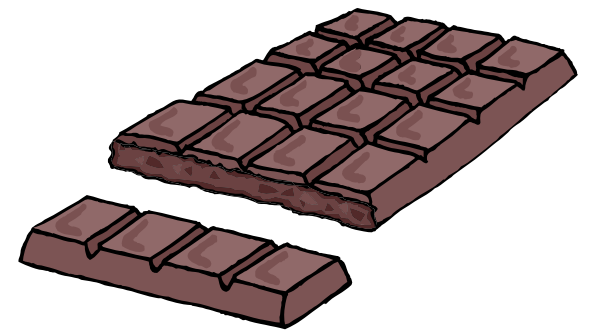
*Kalfon et al, L Neurochem 2007;100:92-1002*

# A role for chocolate in HD?

- Cocoa contains a high concentration of flavenoids. These compounds reduce oxidative damage in animal and cell models.
- Rats fed diets enriched in cocoa extracts were found to have reduced levels of 8OH2'dG (8-hydroxy-2-deoxyguanosine, a marker of oxidative damage to DNA) in the testes and thymus.



*Sources: Orozco et al, J Nutri  
Biochem 2003;14:104-110.  
Ottaviani et al ARch Biochem  
Biophys 2002; 406:203-8.*



# Diet in HD: what can we recommend?

## More research.....in the meantime...

- Eat a diet rich in polyphenol flavinoids (Blue Berries, other fruits, green tea, cocoa).
- Match caloric intake to energy requirements.
- Consider using trehalose or honey in place of sugar.
- ?Role for Turmeric.....need more research
- ?Cholesterol.....need more research

# Supplements in HD

- Coenzyme Q10
- Creatine
- Omega 3 Fatty Acids

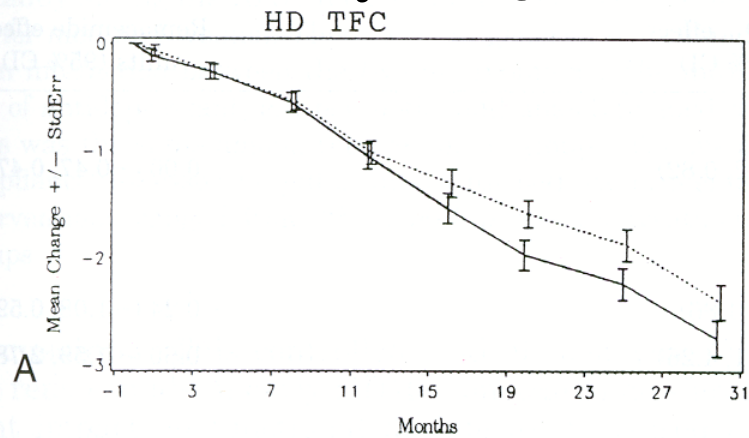
# Coenzyme Q10

- Mechanism: Improves energy metabolism in mitochondria
- Source: occurs in meats and seafood
- Research: benefit seen in HD mouse model, in brain energy metabolism in people with HD, and showed non-significant trend\* of helping slow HD progression in HSG CARE-HD study.

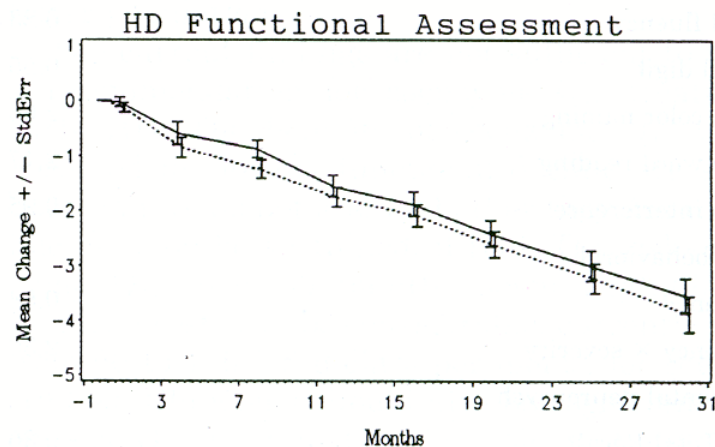
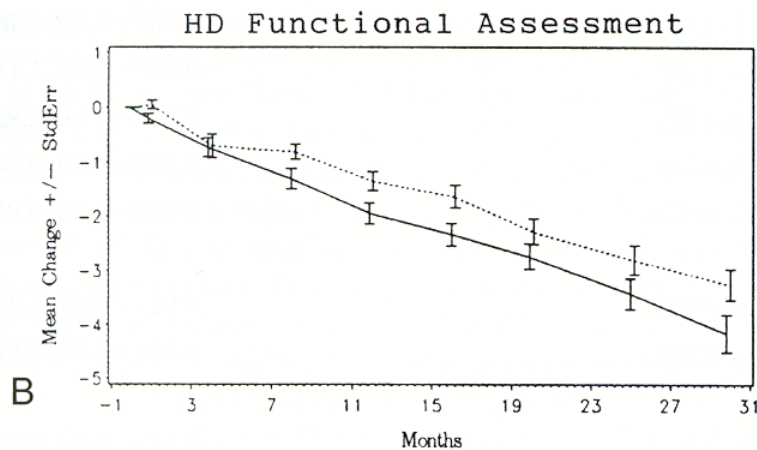
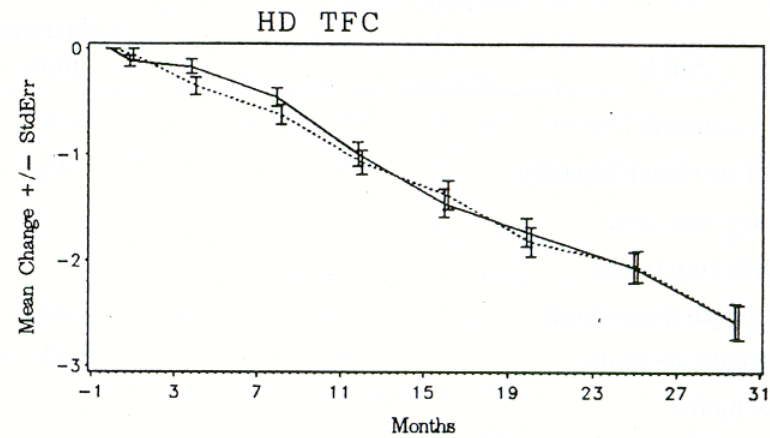
*\***Not** statistically significant. HSG, Neurology 2001;57;397-404*



## Coenzyme Q10



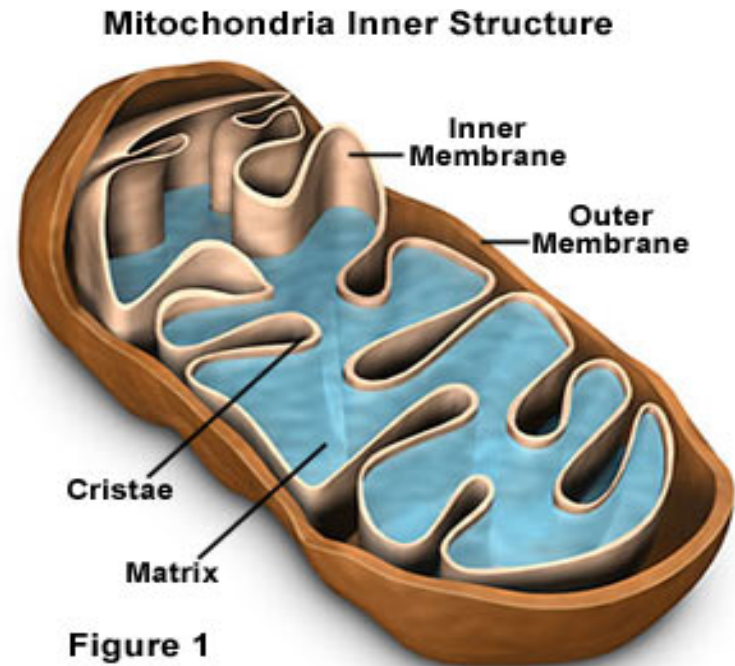
## Remacemide



**Conclusions:** Neither treatment significantly altered decline, however Coenzyme Q10 showed a trend towards slowing of disease progress.  
(HSG, Neurology, 2001)

# Coenzyme Q10

- Dosage: 1200-2400 mg/day
- Safety: established for limited periods.
- Down-side: \$\$\$ (> \$200/month).
- Upcoming 2CARE study: CoQ10
- 2400 mg/d for 5 years, sponsored by NIH.



# Creatine

- Mechanism: improves energy metabolism in body and brain.
- Source: protein-derived.
- Research: improved brain metabolism and decreased blood levels of 8OH-DG; safe and tolerable in people with HD.



# Creatine

- Dose: 5-10 gm/day (possibly more)
- Safety: established at these doses.
- Cost: relatively low.
- Caution: kidney disease, diabetes

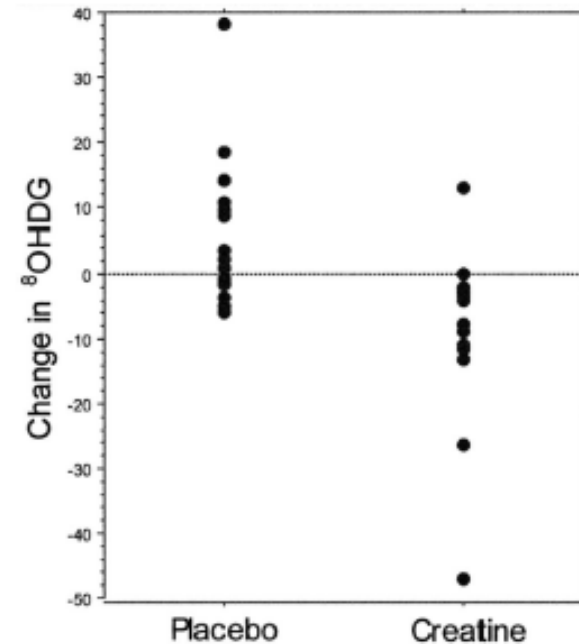
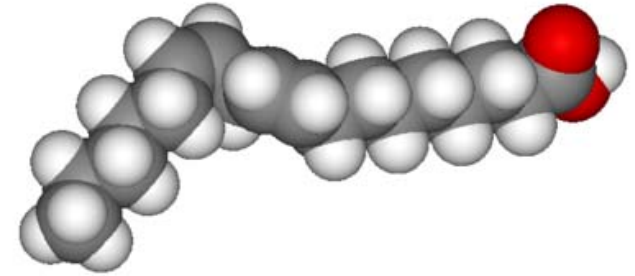


Figure. Changes in serum 8-hydroxy-2'-deoxyguanosine (8OH2'dG) levels in placebo and creatine treated subjects. Scatterplots showing individual changes in 8OH2'dG levels (pg/mL) at week 16 in the 32 subjects from two sites. The difference in the changes between treatment and placebo groups was significant ( $p < 0.0042$ ).

*Hersch et al, Neurology 2006;66:250-2*

# Omega 3 Fatty Acids

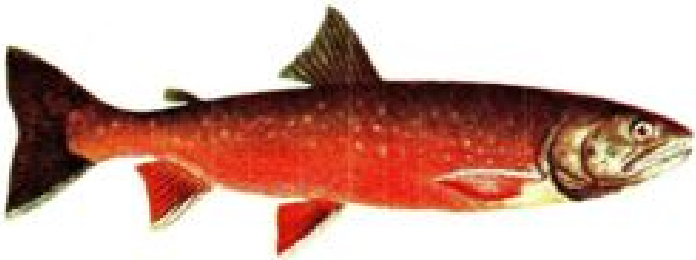


- Mechanism: improves energy metabolism
- Source: seafood, plants (must be obtained from diet)
- Research:
  - Modest help in large European trial.
  - TREND-HD study: didn't help motor score at 6 months; well-tolerated, but 1-year data did suggest some benefit.
- Many participants reported improved mood, well-being



# Omega 3 Fatty Acids

- Dose: 2 or more grams/day fish oil or flaxseed oil
- Safety: established, but beware of mercury contamination.
- Cost: Low
- Caution: blood thinners, avoid falls

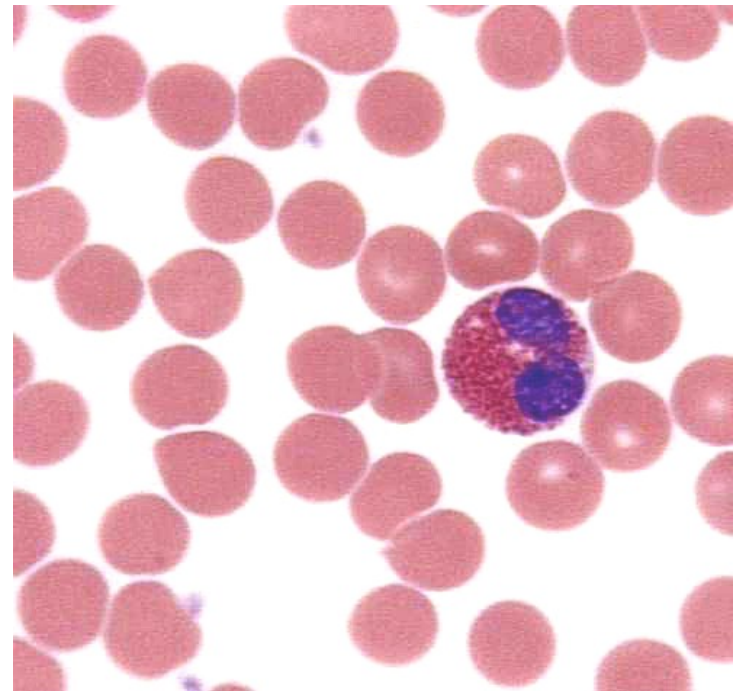


# A few words of caution.

- **Supplements are not FDA regulated.**
  - The L-Tryptophan and eosinophilia myalgia story.
- **We have little data on the long term effects of vitamins and supplements, especially when used at high doses.**
  - The Vitamin E story.
- **Supplements and medications may interact. Use of multiple supplements simultaneously may increase side effects or counteract each other.**
  - The homeopathic consultant and well meaning daughter story.

# “1989 Epidemic of Eosinophilia Myalgia Syndrome”

- L-Tryptophan is sold as a dietary supplement. Purported to aid sleep and depression.
- EMS- is a painful and progressive disease that causes inflammation, scarring and fibrosis in muscle and nerve tissue. Characterized by increases in a type of white blood cell called eosinophils.
- CDC identified > 1,300 cases EMS associated with use of L-Tryptophan (5-HTP) in 1989. Most cases traced to agents from one manufacturing plant in Japan. ( Williamson et al Toxicol Lett 1998: 99)



From: [cellbio.utmb.edu/.../blood/eosinophil1a](http://cellbio.utmb.edu/.../blood/eosinophil1a)



# Vitamin E

- “Meta-Analysis: High-Dosage Vitamin E Supplementation May Increase All-Cause Mortality.” Miller et al., Ann Intern Med 2004: vol 142.
  - 135,967 participants in 19 clinical trials.
  - Vitamin E greater than 400 IU was associated with increase risk of mortality.
  - However, most high dose patients had chronic diseases. Generalizability of findings uncertain.



# **THE HOMEOPATHIC CONSULTANT AND** **THE WELL MEANING DAUGHTER**

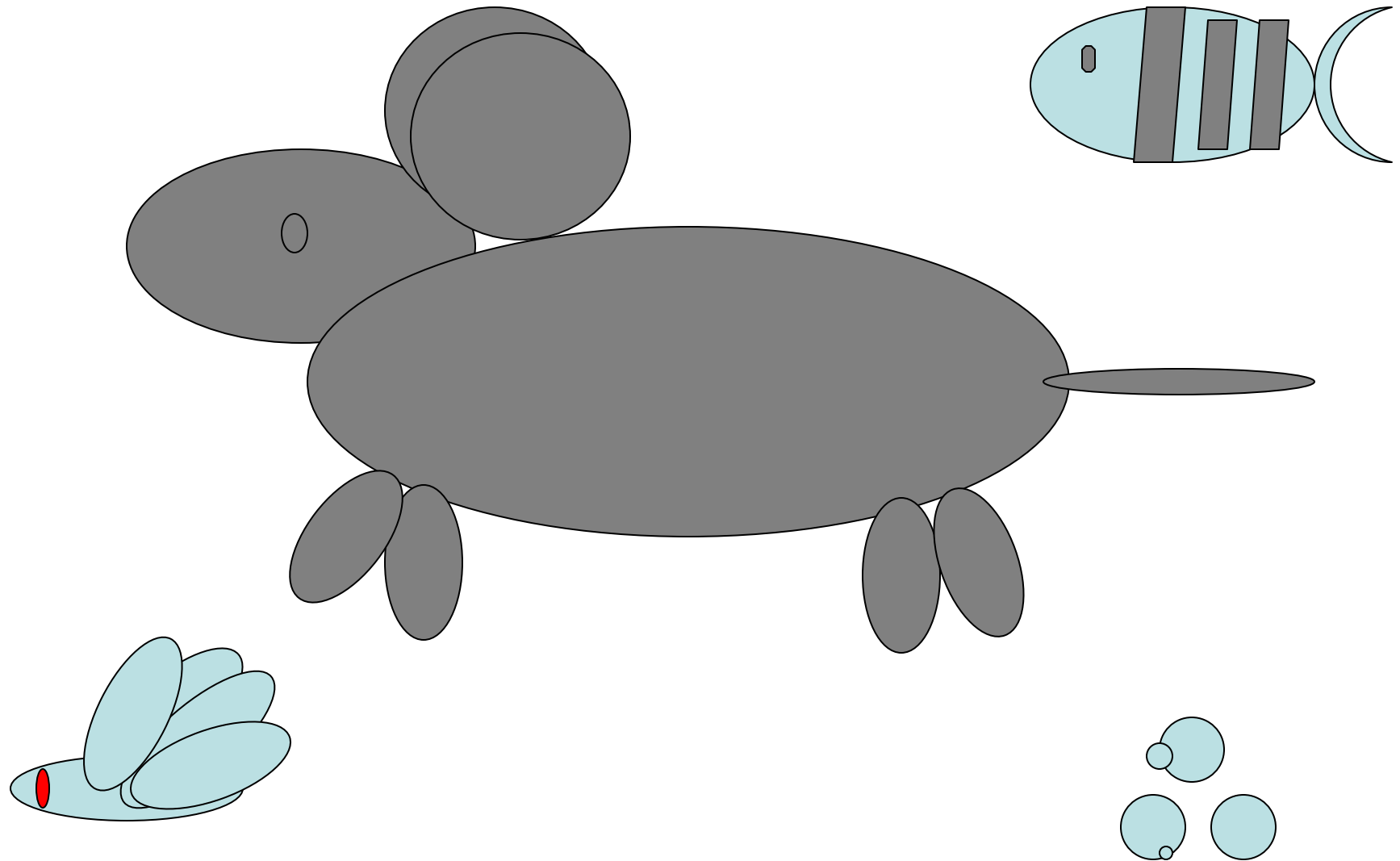
65 year old woman with HD and significant behavioral problems.

Medications: Olanzapine; Valproate Venlafaxine; Buspirone; Clonazepam, Nortriptyline.

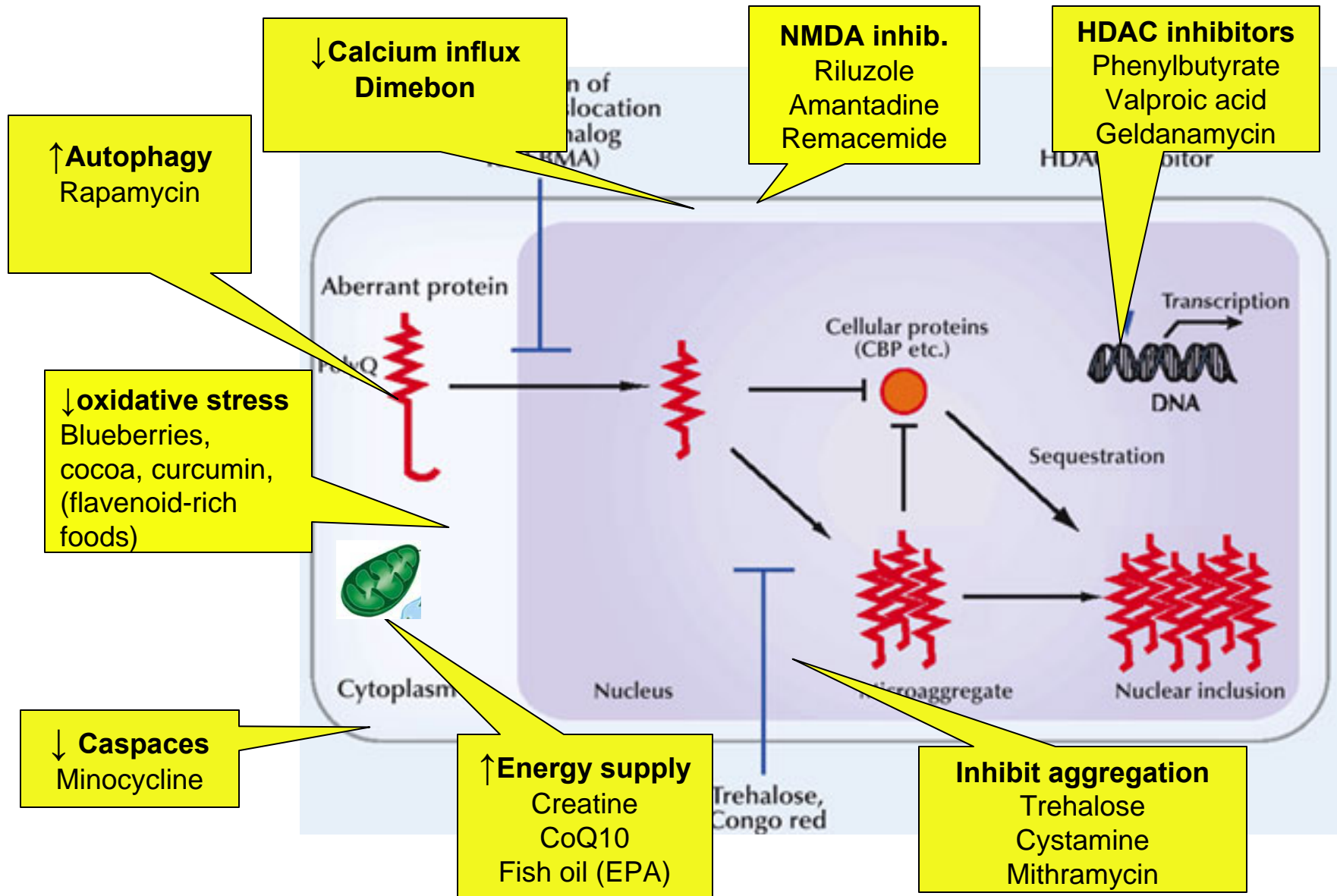
- **Holistic “Supplements” added to daily medications:**
- **“Free radical” drops. 10 drops three times a day.**
- **Maltigen 3 squirts in water in the morning.**
- **“Lymph Drainage” 5 drops three times daily.**
- **“Metox” one drop three times a day**
- **“Sphingolin” twice a day**
- **“UltraDophilus DF” one teaspoon at night**
- **Vitamin B12 one a day, Folic acid one a day, Vitamin B1 one pill in the morning.**
- **Fish oil concentrate 2 tablets per day**
- **Flax seed oil two per day**

**RESULT:** Became obtunded when used in combination with ongoing medications. Lethargy improved within days of stopping supplements.

## Hope for the future: Research in HD



# Multiple HD treatment targets under study



Modified from M Katsuno et al Nature Medicine 10:123, 2004

# Resources for patients and families

[www.HDSA.org](http://www.HDSA.org)

[www.huntingtonproject.org](http://www.huntingtonproject.org)

[www.huntington-study-group.org](http://www.huntington-study-group.org)

[www.hdlighthouse.org](http://www.hdlighthouse.org)

(National Center for Complementary and  
Alternative Medicine.) [www.nccam.nih.gov](http://www.nccam.nih.gov)



Huntington's Disease Society of America

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HDSA encourages all attendees to consult with their primary care provider, neurologist or other healthcare provider about any advice, exercise, medication, treatment, nutritional supplement or regimen that may have been mentioned as part of any presentation.